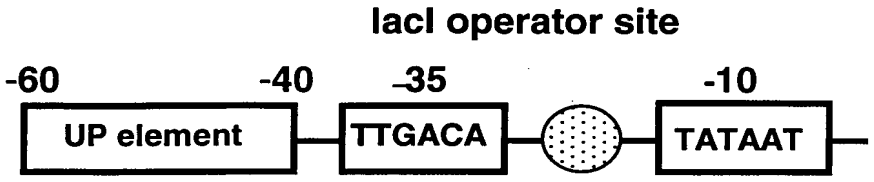


FIG. 1A

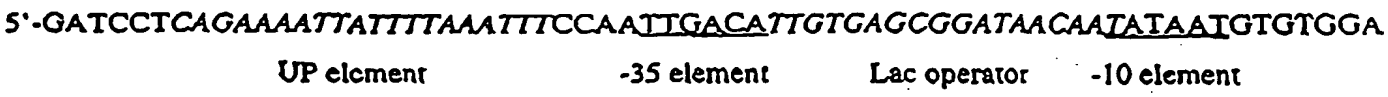

5'-GATCCTCAGAAAATTATTTTAAATTTCCAATTGACATTGTGAGCGGATAACAATATAATGTGTGGA
UP element
-35 element
Lac operator
-10 element

FIG. 1B

5'AGAAAGCAAAAATAAATGCTTGACACTGTAGCGGGAAGGCGTATA
ATGGAATTGTGAGCGGATAACAATTCACA 3'

FIG. 1C

ACTCGCGGA TCATCTTCAC CATCGGCCGC AACTCCTGCG
GGATATCCTC GTCCTCCTCC TCCACCGGCA CCCCCATGGT AGCGGCCAGC
TCGCGCCCTG CCTGGGAAAG CTGTACATGC TGATCGGCGG CGTCGGTGCC
GGCGGCCGGG TCTTCCGCCT GCTCGGCGGT GCCGGTCCGT GCGGCCTTGG
CGTCCGCGGC GGCGCGCGAT GAGGGCGGCA CCTGGGTGGT GATCCAGCCA
CTGAGGGTCA ACATTCCAGT CACTCCGGGA AAAATGGAAT TCTTCCATTG
GATCGGCCCA CGCGTCGCGA ACTTGAGCCC CCTTTTCGTC GCCCCTTGAC
AGGGTGCGAC AGGTAGTCGC AGTTGTTTGA CGCAAGTCAC TGATTGGAAA
CGCCATCGGC CTGTCAGAAA TGGTCGTTGCC AGACCTATGG CTGGCACCCG
CATCGCGGCT GCGTTACCCT TACTCCTGTT GTGCCTTTAA CCTAGCAAGG AC

FIG. 1D

AATTCCTCGA AGTCCTTGCG CTGCTTGTCG TTCATGATGT
CGTAGATCAG CGCATGCACC TGCTTGTGTT CCAGCGGTGG CAGGTTGATC
CGGCGTACAT CGCCATCCAC CCGGATCATG GGTGGCAGGC CGGCGGAGAG
GTGCAGGTCC GAAGCGCCCT GTTTGGCACT GAAGGCGAGC AGCTCGGTAA
TATCCATGGG ACTCCCCAAT TACAAGCAAG CAGGTAGAAT GCCGCCAAAG
CCGCCGTCTC GGACAAGGAA AACACCGGAT GAGCCAGGGT GCTTCCAGGA
CACGCGTGGT GTCCTGCGCC AGACGCGGAA CCTCGACACT GGAACAGGAA
GATGGCCATC GAGGCCGGCG GTTTCGAGGG CGTCGAGCCG ACGCCGACCG
CACTTCCATA GGGCGCAGGT AATGTCCACG ATAGCAGAGA ATATTGCAAA
GGTTGCCGCG CGCATCCGTG AGGCAGCGCA AGCTGCGGGG CGCGATCCGG
CCACGGTCGG CCTGCTCGCC GTGAGCAAGA CCAAGCCCGC CGCCGCGGTG
CGCGAGGCGC ACGCCGCCGG CCTTCGCGAC TTCGGCGAAA ACTACCTGCA
GGAGGCCCTC GGCAAGCAGG CCGAACTGGC CGACCTGCCC TTGAACTGGC
ACTTCATCGG CCCCATCCAG TCGAACAAGA CGCGGCCCAT CGCCGAGCAT
TTCCAGTGGG TGCACTCGGT GGACCGGTTG AAGATCGCGC AGCGCCTGTC
GGAGCAACGC CCGGCCGGGC TGCCGCCCCT GAATGTCTGC CTGCAGGTCA
ACGTCAGCGG CGAAGCCAGC AAGTCCGGCT GCGCCCCCGA GGACCTGCCG
GCCCTGGCCG AGGCCGTGAA GCAACTGCCC AACCTCCGAT TGCGTGGCCT
GATGGCCATC CCCGAACCCA CCGCCGAACG CGCCGCGCAA CACGCCGCGT
TCGCCCGCCT GCGCGAACTG CTGCTGGACC TGAACCTTGG CCTGGACACC
CTGTCCATGG GCATGAGCGA CGACCTCGAG GCAGCCATCGG CGAAGGTGCG
ACCTGGGTCC GCATCGGTAC CGCCCTGTTC GGCGCCCGCGA CTACGGCGCG
CCGGCTTCTT GAATGAATCCC

FIG. 1E

CTAGAGCTAT TGATGTGGAT CAACATTGTC CACTAGCCGC
TGCCGCCTAA TCTCCAGAAT TGTGAG

FIG. 1F

```
   1 ttatttagca ggaataatta gccagattat cgagggagtt ccagggcaatccaaacattg
  61 ttatatatgc atttataaaa ttttcaagat aatttattat tcataccttgccctttgtt
 121 tcaaaattat gccctttttt tgcccttgga aacaaccaca ctcctaaattaataggtggt
 181 gtggtttgat catttataat ataacataaa aacaaccacc cagtaactagtatgagtggc
 241 gtagcgacta taacaactct atgttatcaa gatatatgta tatgagtgatgacaaggaag
 301 atgtctcctg tgagaccaac agccagatat atggcctctt gccgggctatatagttcact
 361 cctactatat acacatgtaa ttataacata aaaaaataga caagtaccgaagtacctgcc
 421 taaataacaa caagattaac atgtgaataa tggaaataaa aagtcagcccgaaggctaac
 481 ttacgaatag atgaaaattt gaacacattg ctgtgtctaa aatgattatagcataaataa
 541 cgaatatttc cagctcgaaa ttaatatatt gtaataataa tattttatatctttgttaat
 601 aattatttaa ttgatttaca taaataataa ttgtaaaatt aatttgtaatcgattgcaaa
 661 taagttatag gagaaaataa aatgaataaa aaactattaa caaaaacattgatagcaagt
 721 gctttagttt taacaacagt aggttcaggt tttcattctt cttcaaattataatggtatt
 781 aataacgttg aaaaagctga gcaaacgaca gataacgcat tgtggaaaaatgtaagagac
 841 gctttaaaag acgcgaatat tatcgataaa acagataatg aaaatgtcaaggttacgtat
 901 aaaatagaaa atggtggaga aaataccata gaaggaacag ttaatttagaaaatattagt
 961 acttcaaaca atcctaaaat aaaccctcaa aatgttacaa aaattaatataactagaaaa
1021 aatccgaact accctaatat tgatgctaat aatacatgga aaaaattaccagaaaaattg
1081 aaagaaaaaa atatagtgga acaacggcga caatgtttca atcttaagtacagaccctaa
1141 agatgagact gtattcggta aagtaggaga agataaatca aacgtaagcaatagatacat
1201 caatcctaaa gatataaatg aattcaaatc actaaaaata ctttttccgaggcagatta
1261 ctcctgcctc tttctttgaa cagtgatatc ttctgatcta tgtaacactcaattacttca
1321 gattctttac ctttaacttc ctttaattca tttctctcta tctcctcaaaaagttgtgct
1381 ttttgatttg tgattggagt tgggcgtttt ttcatcgcgt tgtttcaattccttttaag
1441 gtattctaat tctcttctag tcatatcaat tgtttttta cttctcacctttagtgaaat
1501 actcttatcc tttctcttct tgcgttaatg ttgctaatta gtataaaatacatgcgccca
1561 tatattccaa tggtaggaca tttaattctg gattttcagc tattttcataaatctattat
1621 ctgataattt gcttaatcca attttcaagc catagcctaa attccccatccactaagtca
1681 ttttgtttca tatggtttta atctacggcc aatctcaaag atagattgaccagcgatgtt
1741 taaagtcata tttcacggat ccacatttac gataaacata tctagttacacaatattatc
1801 ccttactgca acacaggacg tttctcagcg taaaaaacac cactagaaagtgactttaaa
1861 gaatataact aattcaaact tatattaatt aatattcttt aaatgaccactcacactttg
1921 ttttttgcta tttgtaactt taaaatgttg tttgaaatct atatttttttgatatagctc
1981 cctatgtaac aaacaatttt taattaatat atatttaaac aagtcaatttagagatcggt
2041 taattcgatt catttaaata atatttatac attctatatg taaacgtttacacatttgaa
2101 gtaaggagaa ttaaaaatga
```

FIG. 1G

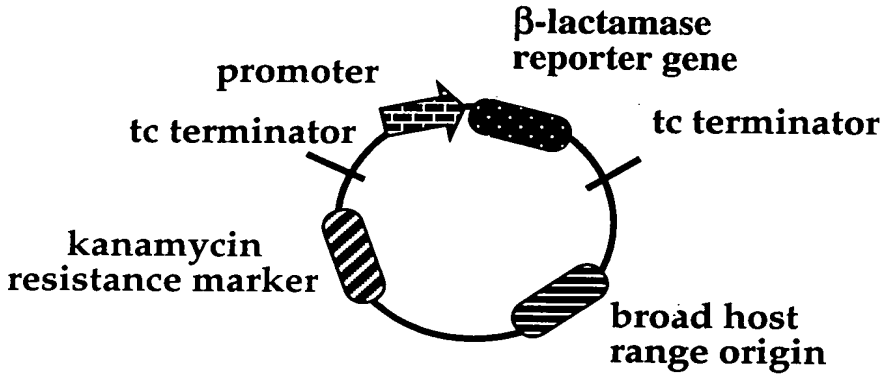


Figure 2. β-Lactamase Reporter Plasmid.

FIG. 2

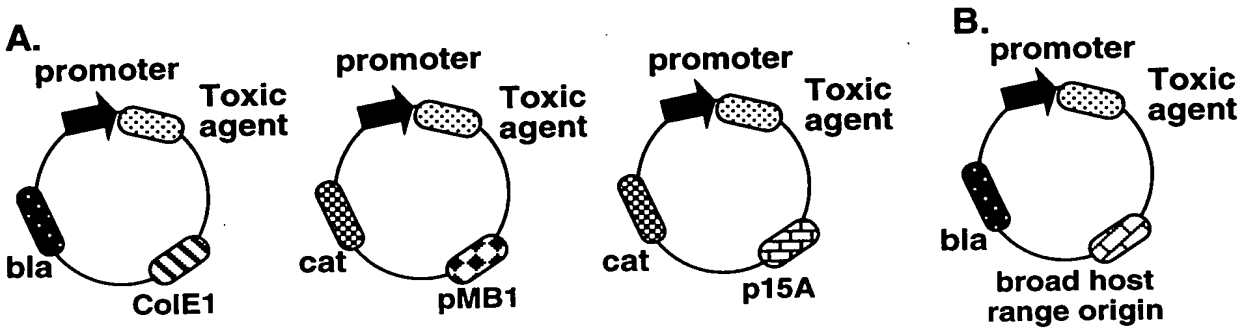

A.
promoter
Toxic agent
bla
ColE1
promoter
Toxic agent
cat
pMB1
promoter
Toxic agent
cat
p15A
B.
promoter
Toxic agent
bla
broad host range origin

FIG. 3

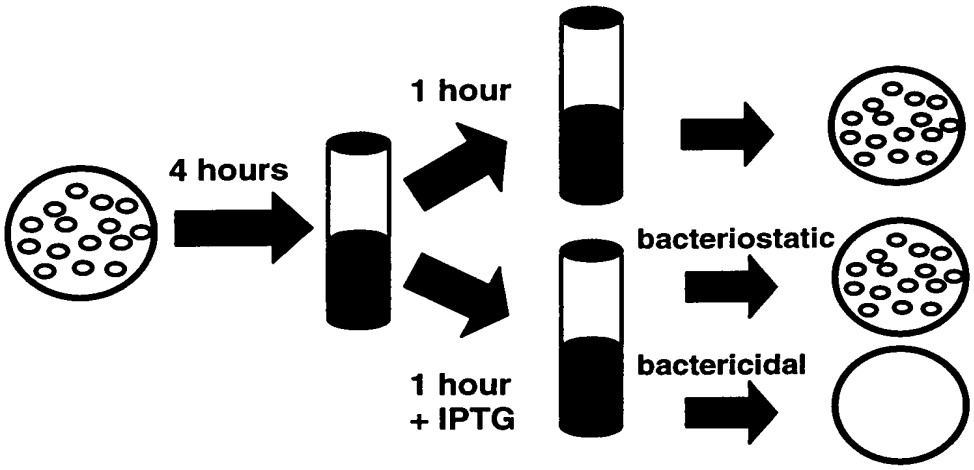


FIG. 4

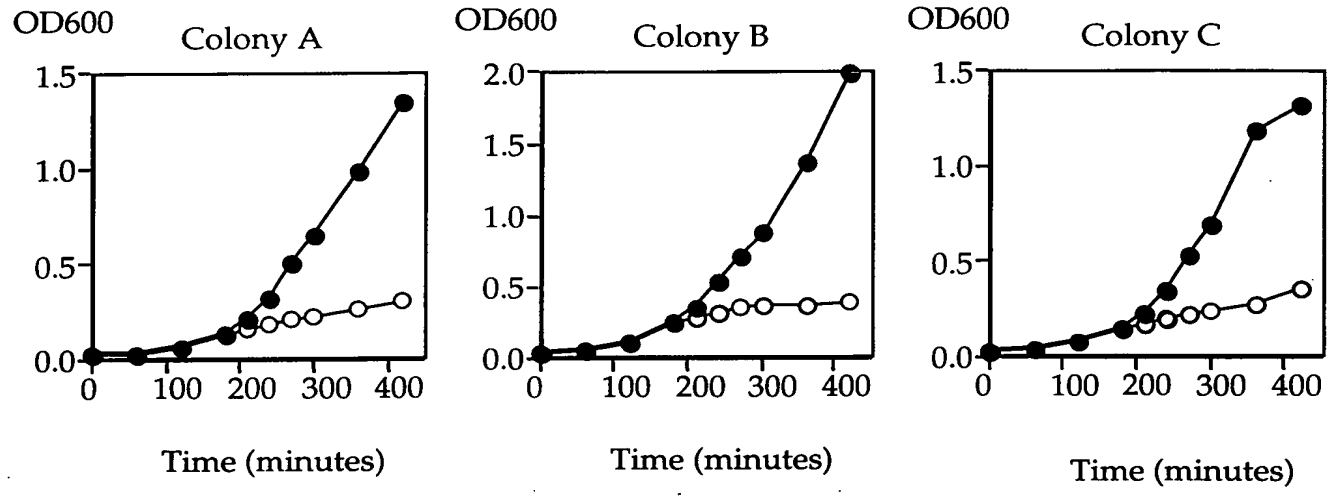

OD600
Colony A
1.5
1.0
0.5
0.0
0
100
200
300
400
Time (minutes)
OD600
Colony B
2.0
1.5
1.0
0.5
0.0
0
100
200
300
400
Time (minutes)
OD600
Colony C
1.5
1.0
0.5
0.0
0
100
200
300
400
Time (minutes)

FIG. 5

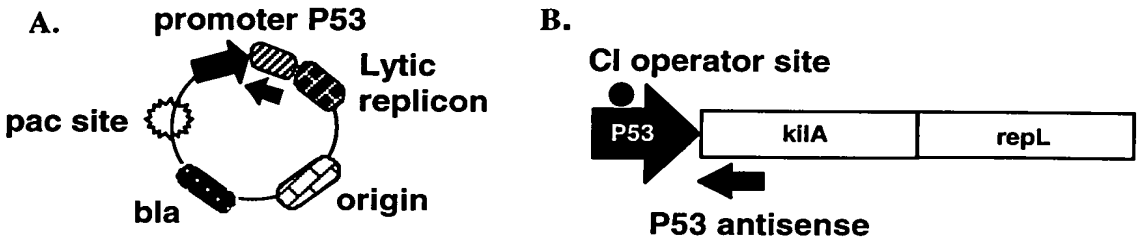

A.
promoter P53
Lytic replicon
pac site
bla
origin
B.
CI operator site
P53
kilA
repL
P53 antisense

FIG. 6

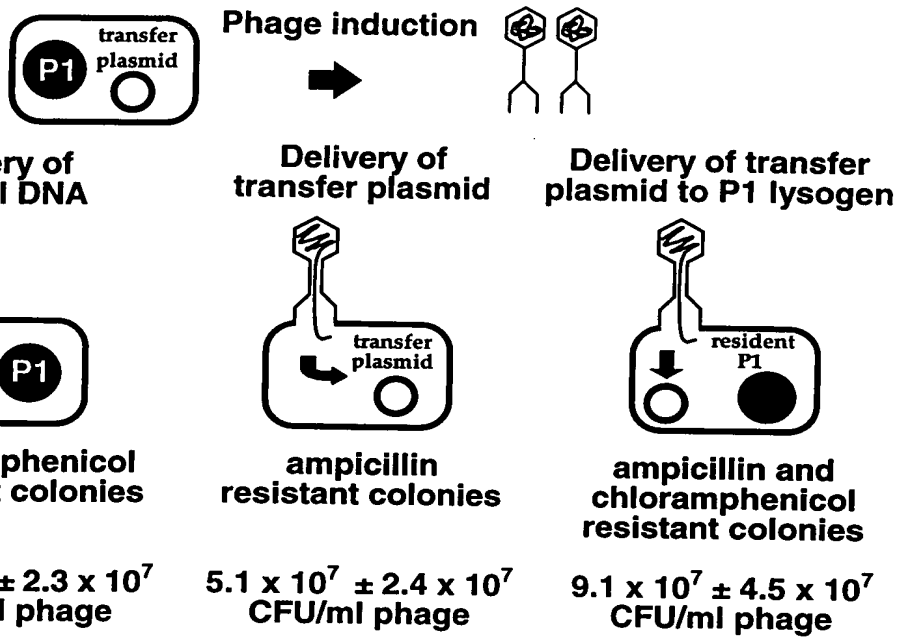

transfer plasmid
P1
Phage induction
Delivery of P1 viral DNA
Delivery of transfer plasmid
Delivery of transfer plasmid to P1 lysogen
P1
transfer plasmid
resident P1
chloramphenicol resistant colonies
ampicillin resistant colonies
ampicillin and chloramphenicol resistant colonies
9.3 x 10^7 ± 2.3 x 10^7 CFU/ml phage
5.1 x 10^7 ± 2.4 x 10^7 CFU/ml phage
9.1 x 10^7 ± 4.5 x 10^7 CFU/ml phage

FIG. 7

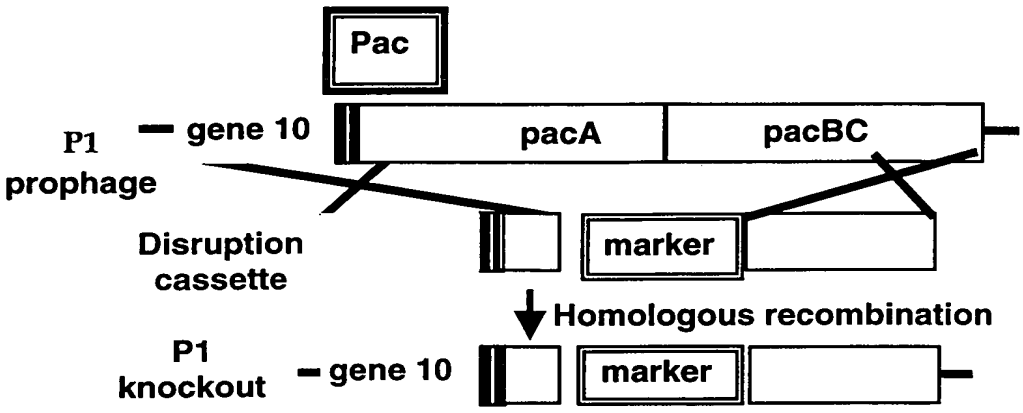

Pac
P1
prophage
gene 10
pacA
pacBC
Disruption
cassette
marker
Homologous recombination
P1
knockout
gene 10
marker

FIG. 8

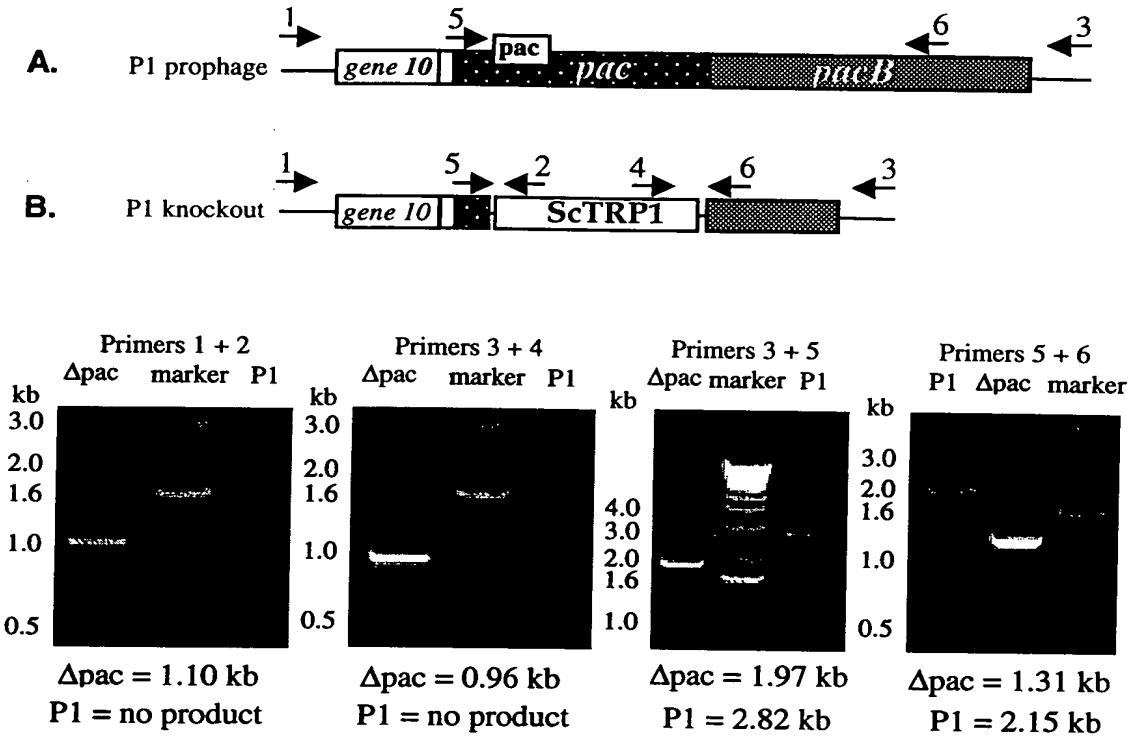

A.
P1 prophage
1
5
6
3
gene 10
pac
pac
pacB
B.
P1 knockout
1
5
2
4
6
3
gene 10
ScTRP1
Primers 1 + 2
Δpac marker P1
kb
3.0
2.0
1.6
1.0
0.5
Δpac = 1.10 kb
P1 = no product
Primers 3 + 4
Δpac marker P1
kb
3.0
2.0
1.6
1.0
0.5
Δpac = 0.96 kb
P1 = no product
Primers 3 + 5
Δpac marker P1
kb
4.0
3.0
2.0
1.6
1.0
Δpac = 1.97 kb
P1 = 2.82 kb
Primers 5 + 6
P1 Δpac marker
kb
3.0
2.0
1.6
1.0
0.5
Δpac = 1.31 kb
P1 = 2.15 kb

FIG. 9

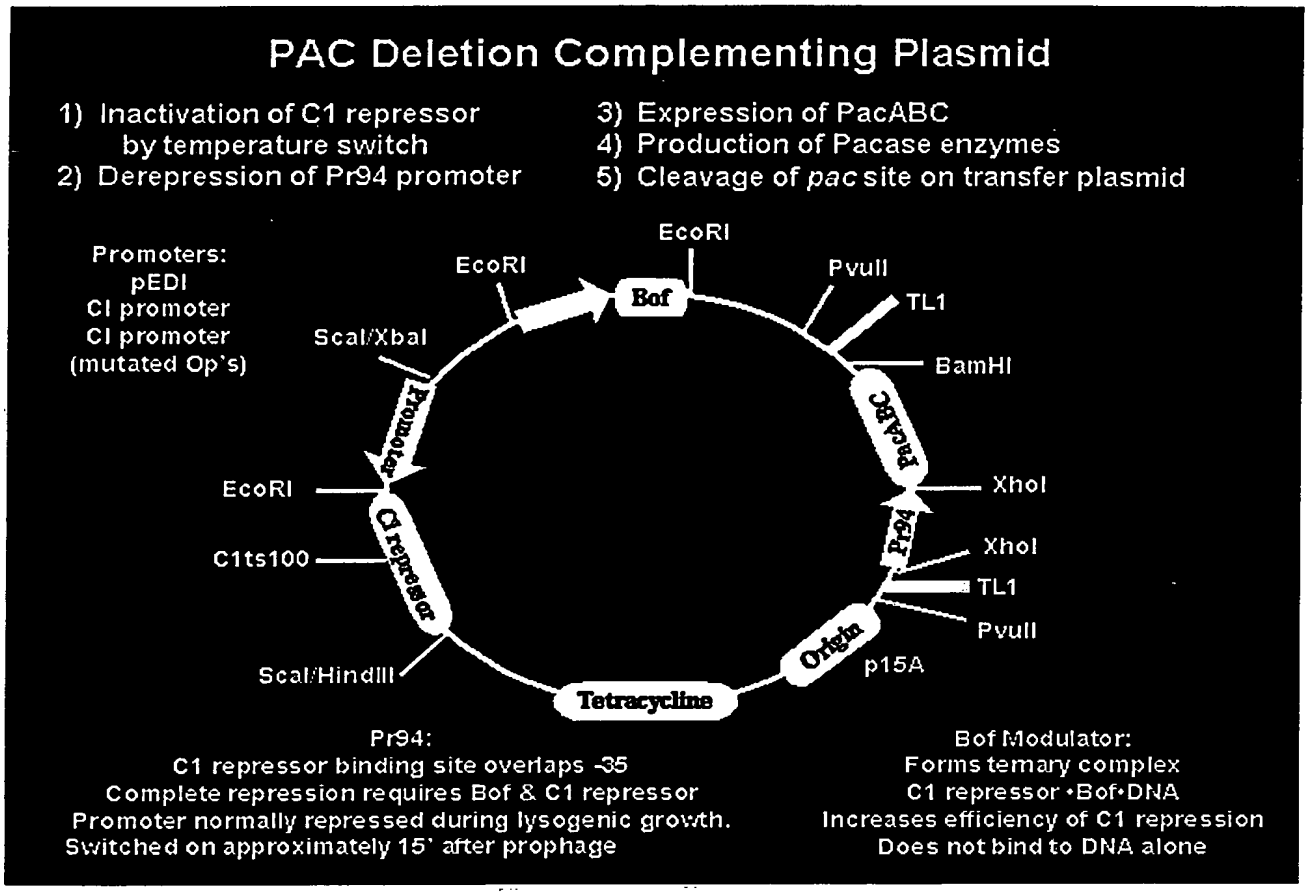

PAC Deletion Complementing Plasmid
1) Inactivation of C1 repressor by temperature switch
2) Derepression of Pr94 promoter
3) Expression of PacABC
4) Production of Pacase enzymes
5) Cleavage of pac site on transfer plasmid
Promoters:
pEDI
CI promoter
CI promoter
(mutated Op's)
EcoRI
Bof
PvuII
TL1
BamHI
PacABC
XhoI
Pr94
XhoI
TL1
PvuII
p15A
Origin
Tetracycline
ScaI/HindIII
C1ts100
EcoRI
CI repressor
Promoter
ScaI/XbaI
EcoRI
Pr94:
C1 repressor binding site overlaps -35
Complete repression requires Bof & C1 repressor
Promoter normally repressed during lysogenic growth.
Switched on approximately 15' after prophage
Bof Modulator:
Forms ternary complex
C1 repressor•Bof•DNA
Increases efficiency of C1 repression
Does not bind to DNA alone

FIG.10

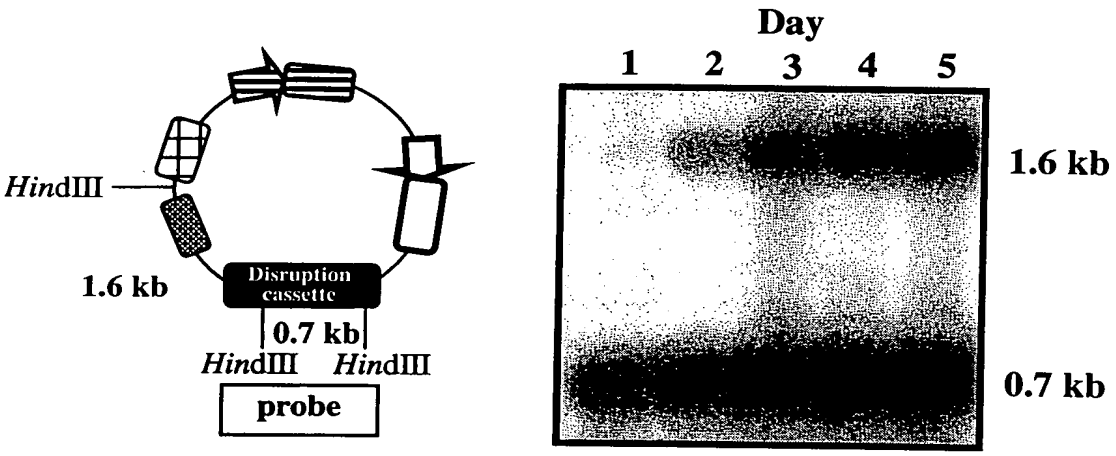

HindIII
1.6 kb
Disruption cassette
0.7 kb
HindIII
HindIII
probe
Day
1
2
3
4
5
1.6 kb
0.7 kb

FIG.11

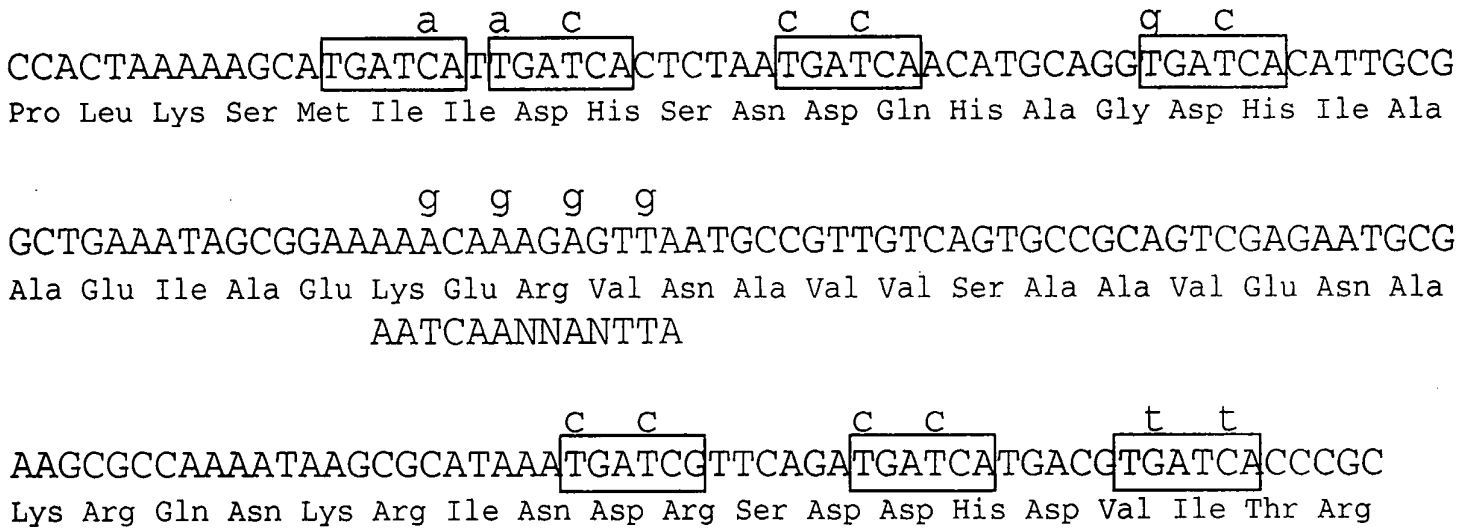

a a c c c g c
CCACTAAAAAGCATGATCATTGATCACTCTAATGATCAACATGCAGGTGATCACATTGCG
Pro Leu Lys Ser Met Ile Ile Asp His Ser Asn Asp Gln His Ala Gly Asp His Ile Ala
g g g g
GCTGAAATAGCGGAAAAACAAAGAGTTAATGCCGTTGTCAGTGCCGCAGTCGAGAATGCG
Ala Glu Ile Ala Glu Lys Glu Arg Val Asn Ala Val Val Ser Ala Ala Val Glu Asn Ala
AATCAANNANTTA
c c c c t t
AAGCGCCAAAATAAGCGCATAAATGATCGTTCAGATGATCATGACGTGATCACCCGC
Lys Arg Gln Asn Lys Arg Ile Asn Asp Arg Ser Asp Asp His Asp Val Ile Thr Arg

FIG.12

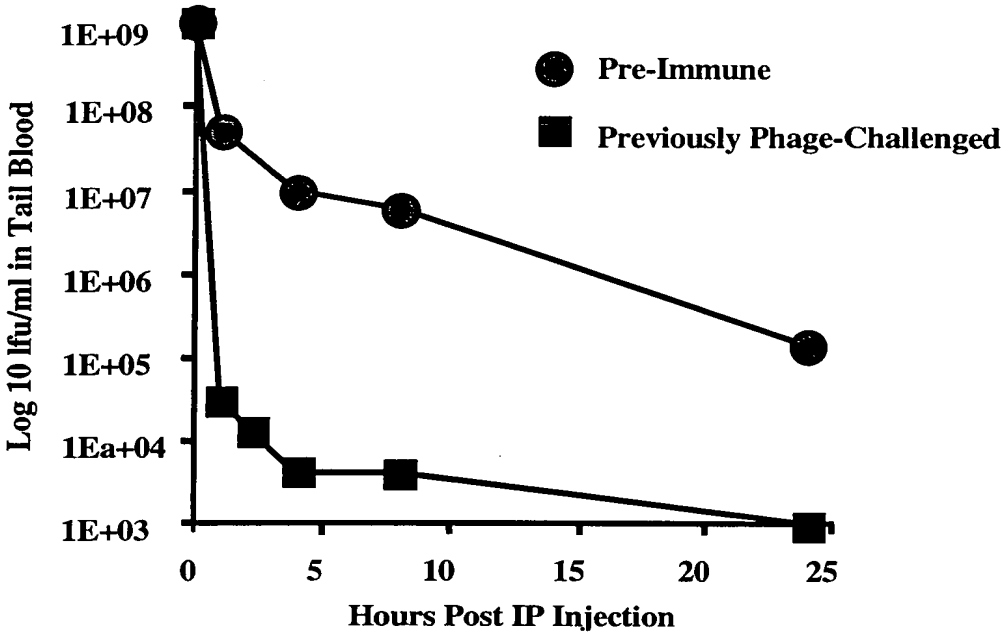
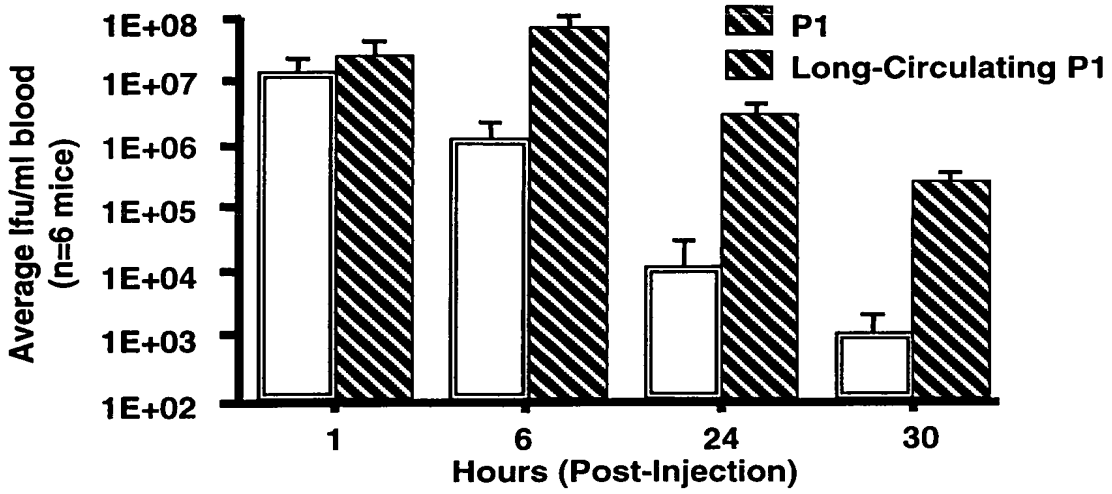

1E+09
1E+08
1E+07
1E+06
1E+05
1Ea+04
1E+03
Log 10 lfu/ml in Tail Blood
0
5
10
15
20
25
Hours Post IP Injection
Pre-Immune
Previously Phage-Challenged

FIG.13



Hours Post-Injection	P1 (mean Ifu/ml blood)	Long-Circulating P1 (mean Ifu/ml blood)	Fold Improvement
1	1.29E + 07	2.34E + 07	2
6	1.13E + 06	6.29E + 07	56
24	1.12E + 04	2.79E + 06	249
30	1.00E + 03	2.33E + 05	233

FIG.14

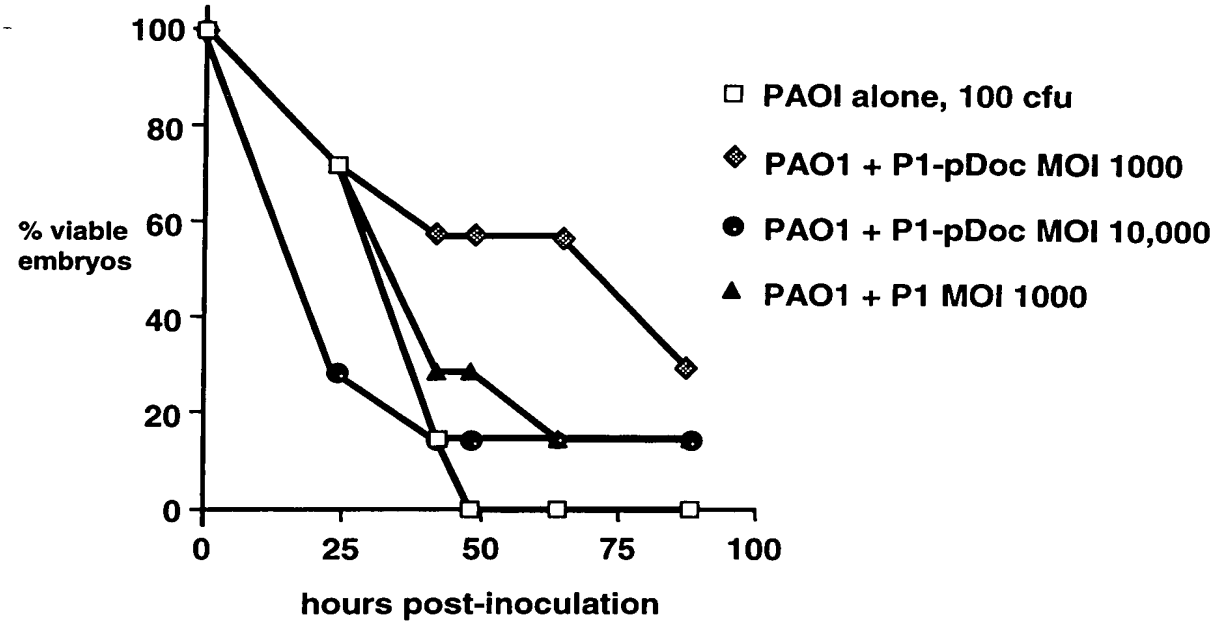

100
80
60
40
20
0
% viable embryos
0
25
50
75
100
hours post-inoculation
PAOI alone, 100 cfu
PAO1 + P1-pDoc MOI 1000
PAO1 + P1-pDoc MOI 10,000
PAO1 + P1 MOI 1000

FIG.15

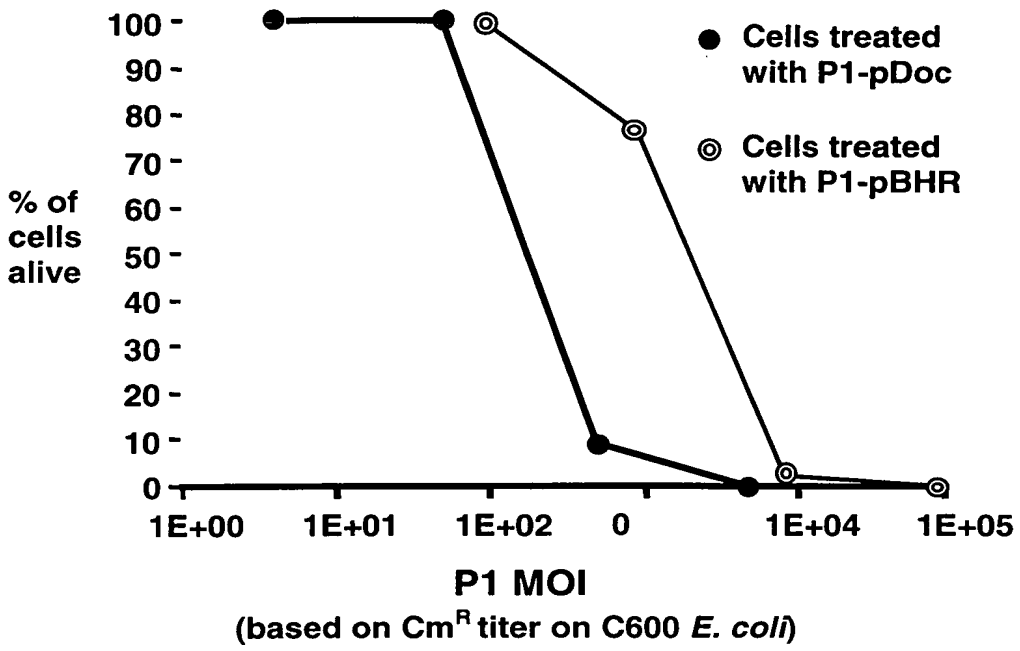

100
90
80
70
60
50
40
30
20
10
0
% of cells alive
Cells treated with P1-pDoc
Cells treated with P1-pBHR
1E+00
1E+01
1E+02
0
1E+04
1E+05
P1 MOI
(based on Cm^R titer on C600 E. coli)

FIG. 16

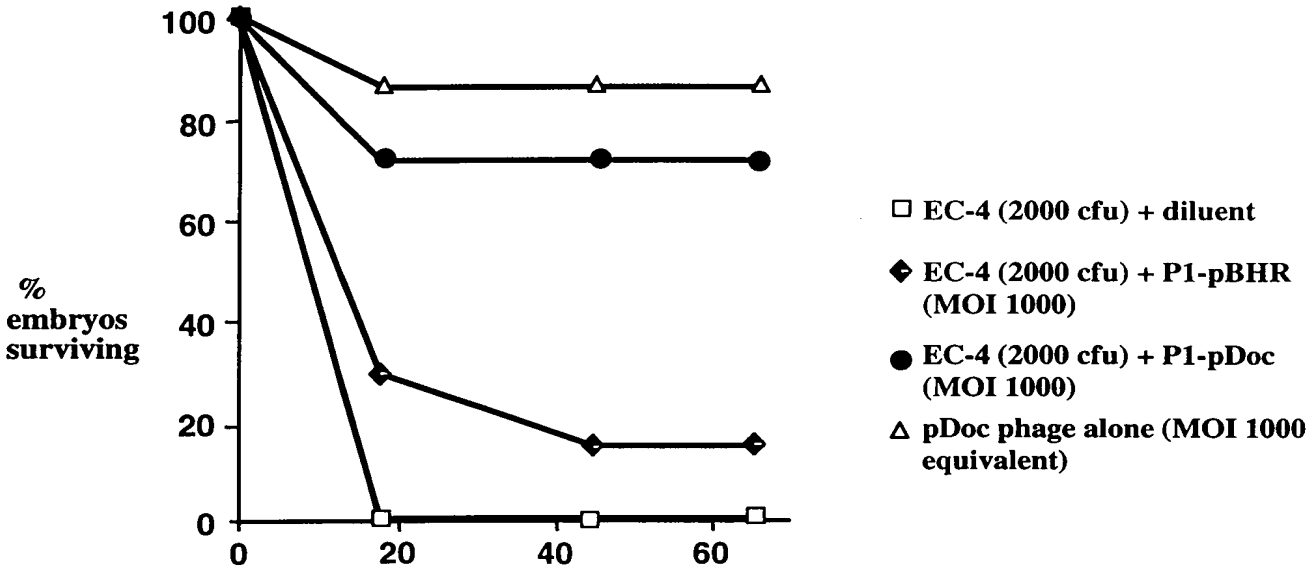

100
80
60
40
20
0
0
20
40
60
% embryos surviving
EC-4 (2000 cfu) + diluent
EC-4 (2000 cfu) + P1-pBHR (MOI 1000)
EC-4 (2000 cfu) + P1-pDoc (MOI 1000)
pDoc phage alone (MOI 1000 equivalent)

FIG. 17

5'-CAGGCGACAGGTATAGTTTCTCTCCGATTTGTGCCTGTCGCCTGC

FIG. 18

pClip Triple Ribozyme Structure

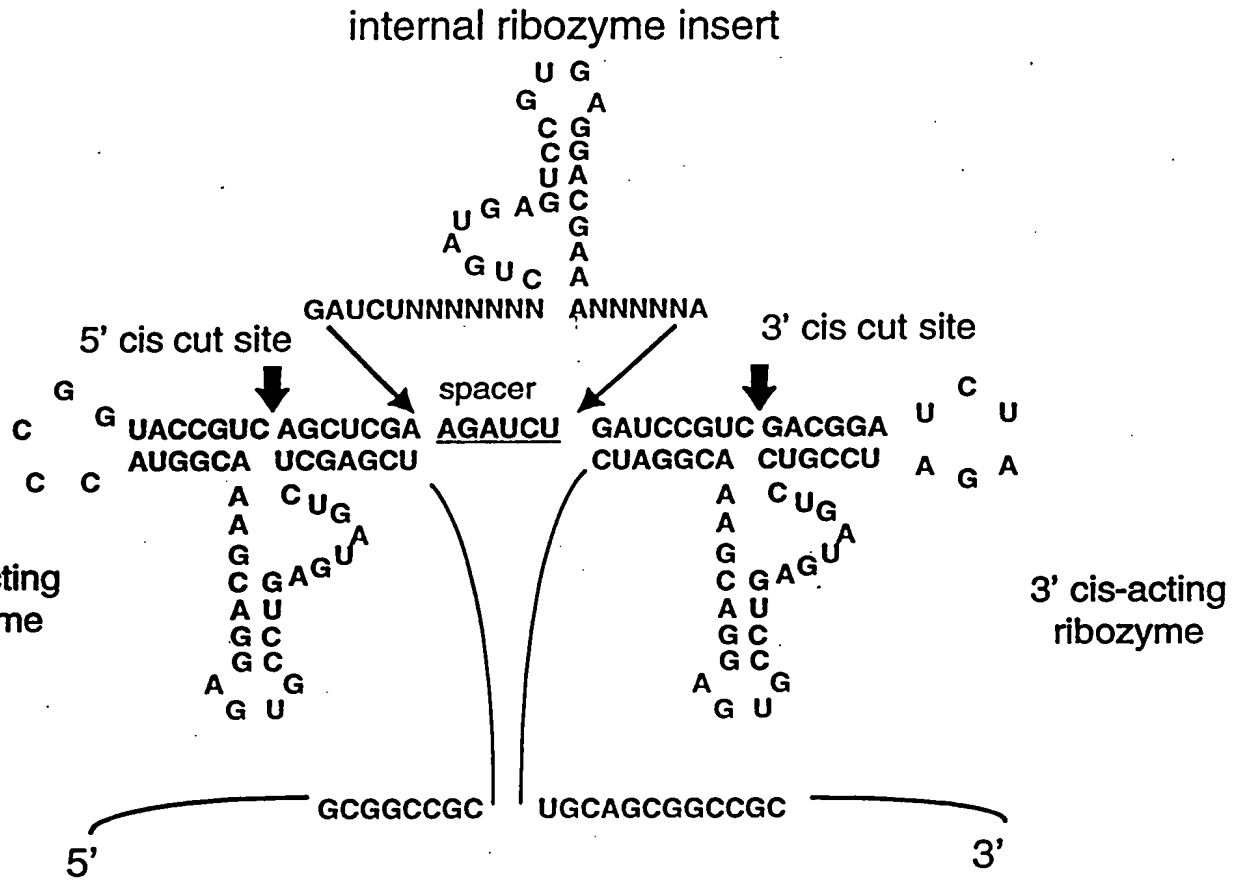


FIG. 19

pChop Triple Ribozyme Structure

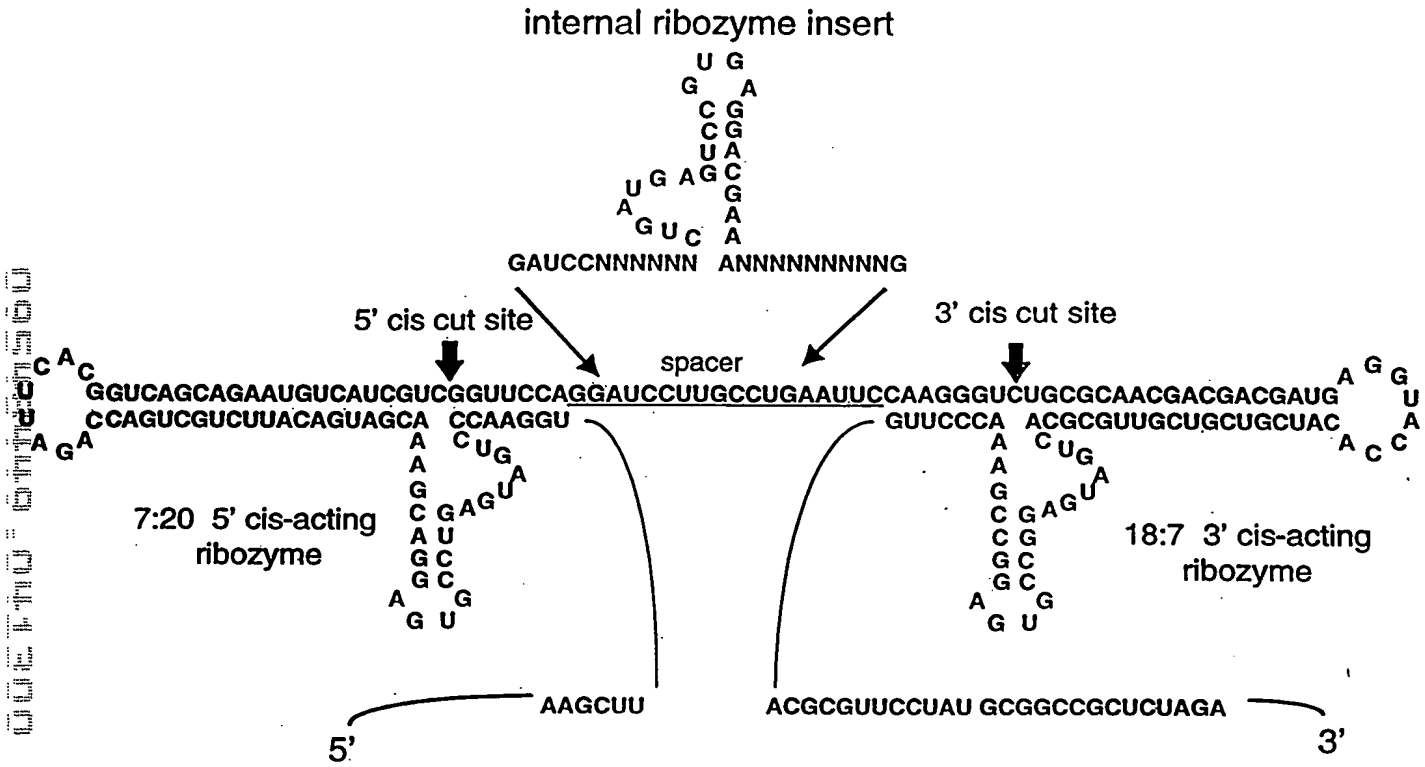


FIG. 20

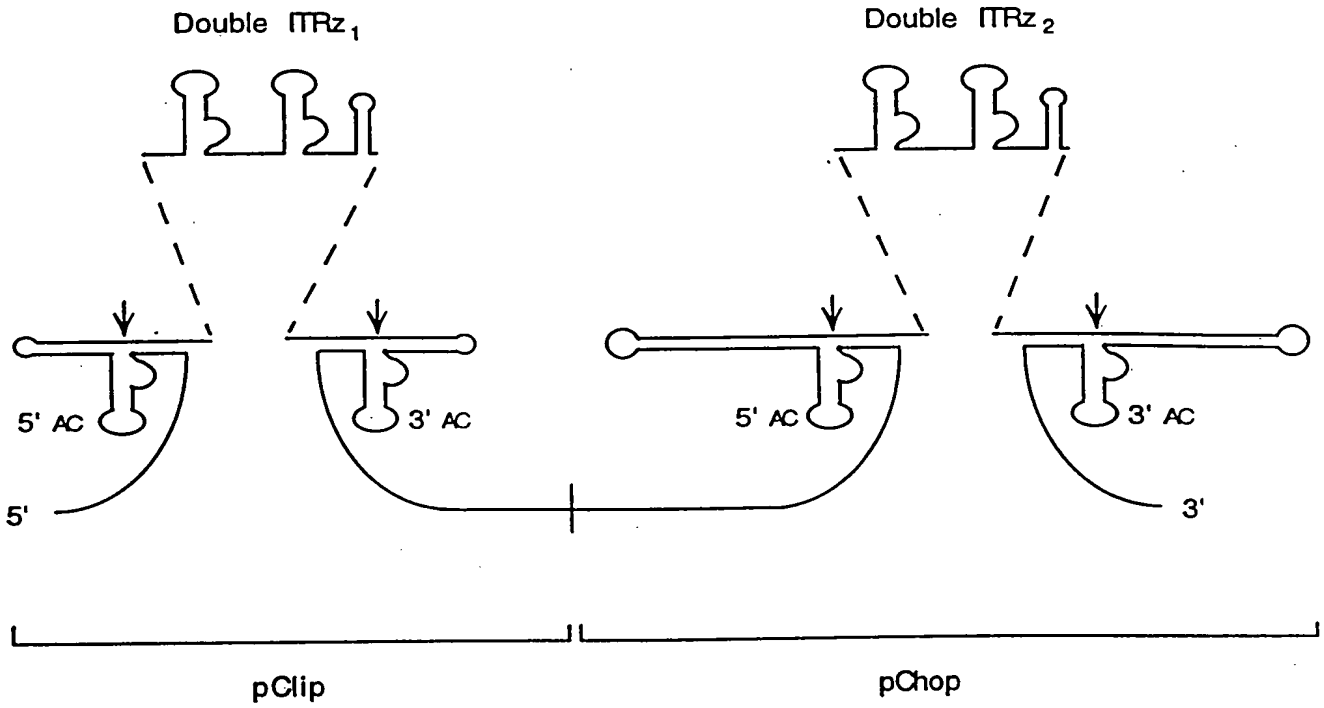


FIG. 21

FIG. 22A

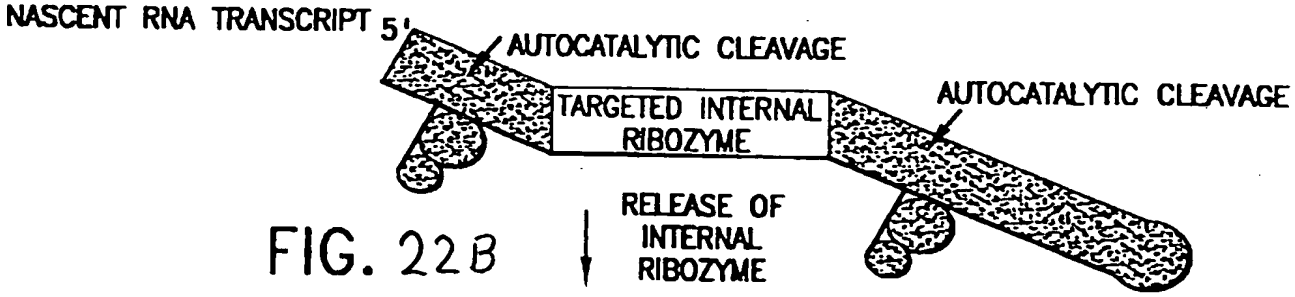


FIG. 22B

RELEASE OF INTERNAL RIBOZYME

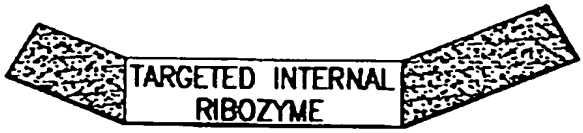


FIG. 22C

SEQUENCE SPECIFIC HYBRIDIZATION

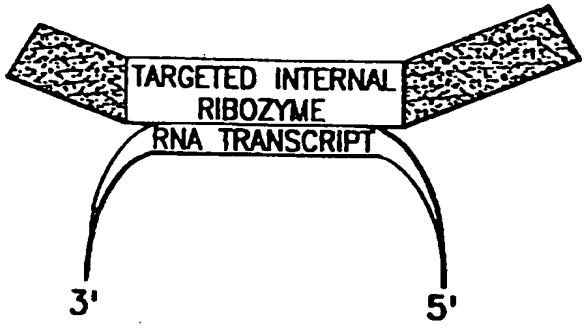


FIG. 22D

TRANS-CATALYTIC CLEAVAGE

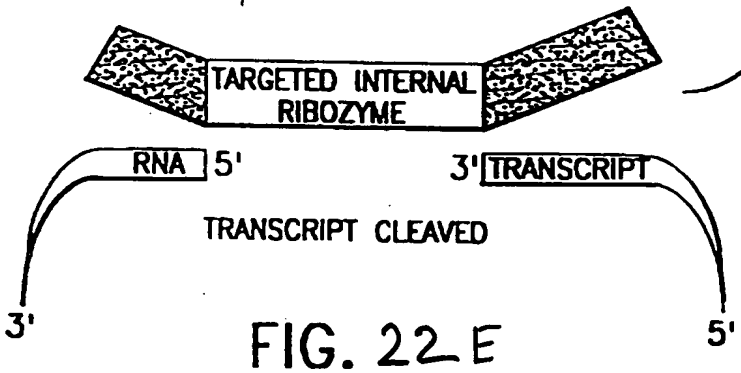


FIG. 22E